



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 148531

TO: Abdel Mohamed
Location: rem/3b79/3c70
Art Unit: 1653
Monday, March 28, 2005

Case Serial Number: 10/036918

From: Alex Waclawiw
Location: Biotech-Chem Library
CM1-6A02
Phone: 308-4491

Alexandra.waclawiw@uspto.gov

Search Notes

CRFF

Access DB# 148581

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: ABDEL MOHAMED Examiner #: 66323 Date: 03/22/05
Ext Unit: 1653 Phone Number #: 212-0955 Serial Number: 101036, 918
Mail Box and Bldg/Room Location: REM3 B79 Results Format Preferred (circle): PAPER DISK E-MAIL
REM3 C70

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____ SP

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search SEQ ID NO 4

aa-8

Thanks
Abdel

MEJ

STAFF USE ONLY

Searcher:	Point of Contact:	Type of Search	Vendors and cost where applicable
Searcher Phone #:	<u>Alexandra Wacławiw</u>	NA Sequence (#) _____	STN _____
Searcher Location:	<u>Technical Info. Specialist</u>	AA Sequence (#) <u>1</u>	Dialog _____
Date Searcher Picked Up:	<u>3-28</u>	Structure (#) _____	Questel/Orbit _____
Date Completed:	<u>3-28</u>	Bibliographic _____	Dr.Link _____
Searcher Prep & Review Time:	<u>15</u>	Litigation _____	Lexis/Nexis _____
Critical Prep Time:	_____	Fulltext _____	Sequence Systems _____
Online Time:	<u>25</u>	Patent Family _____	WWW/Internet _____
		Other _____	Other (specify) <u>CompuLink</u>

=> d his

(FILE 'HOME' ENTERED AT 13:47:39 ON 28 MAR 2005)

FILE 'REGISTRY' ENTERED AT 13:47:45 ON 28 MAR 2005

L1 0 S GPGRPYGL/SQSP
L2 714 S .P.RPY.L/SQSP
L3 44 S L2 AND PIPERID?
E PIPERIDIN/CN
E PIPERIDINE/CN
L4 1 S E3
L5 2127679 S NC5/ES
L6 45 S L5 AND L2
L7 7 S L6 AND SQL=8

FILE 'HCAPLUS' ENTERED AT 13:50:39 ON 28 MAR 2005

L8 2 S L7

=> fil reg
FILE 'REGISTRY' ENTERED AT 13:51:18 ON 28 MAR 2005
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES: 27 MAR 2005 HIGHEST RN 847353-93-9
DICTIONARY FILE UPDATES: 27 MAR 2005 HIGHEST RN 847353-93-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d que 17
L2 714 SEA FILE=REGISTRY ABB=ON PLU=ON .P.RPY.L/SQSP
L5 2127679 SEA FILE=REGISTRY ABB=ON PLU=ON NC5/ES
L6 45 SEA FILE=REGISTRY ABB=ON PLU=ON L5 AND L2
L7 7 SEA FILE=REGISTRY ABB=ON PLU=ON L6 AND SQL=8

=> d sqide3 17 1-7

L7 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN
RN 694452-76-1 REGISTRY
CN L-Leucine, (2S)-2-(4-piperidinyl)-N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-
tetraazacyclododec-1-yl]acetyl]glycyl-L-prolyl-(2S)-2-[1-
(aminoiminomethyl)-4-piperidinyl]glycyl-L-arginyl-L-prolyl-L-tyrosyl-3-
methyl-L-valyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 8
NTE modified (modifications unspecified)

SEQ3 1 Gly-Pro-Gly-Arg-Pro-Tyr-Val-Leu
=== === === === ===
HITS AT: 1-8

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C68 H111 N19 O17

SR CA

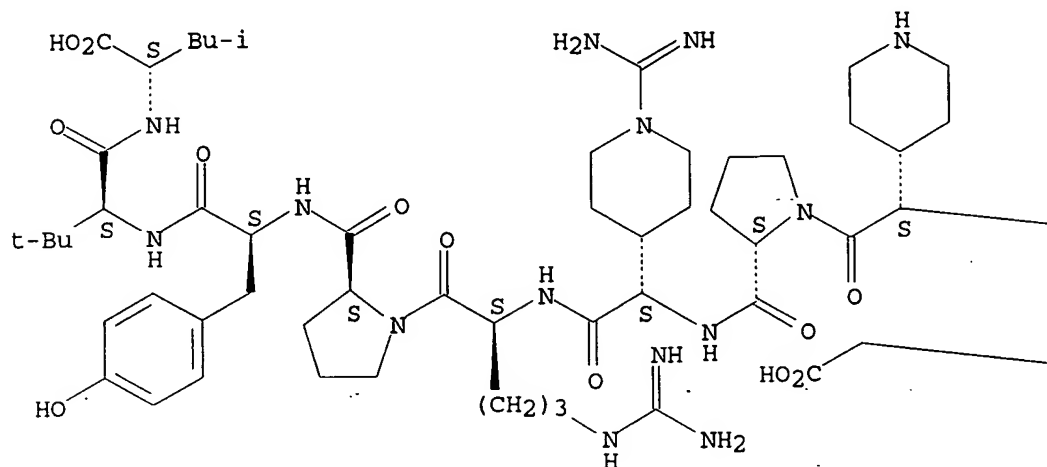
LC STN Files: CA, CAPLUS

DT.CA CAPLUS document type: Journal

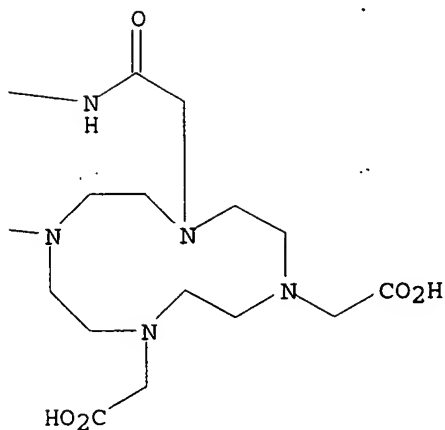
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L7 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN
RN 579449-02-8 REGISTRY
CN L-Leucine, (2S)-N-[[[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5(or 6)-yl]amino]thioxomethyl]-2-[1-[[[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5(or 6)-yl]amino]thioxomethyl]-4-piperidinyl]glycyl-L-prolyl-(2S)-2-[1-(aminoiminomethyl)-4-piperidinyl]glycyl-L-arginyl-L-prolyl-L-tyrosyl-3-methyl-L-valyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 8
NTE modified (modifications unspecified)

SEQ3 1 Gly-Pro-Gly-Arg-Pro-Tyr-Val-Leu .
=== === === === === === ===
HITS AT: 1-8

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C94 H107 N17 O20 S2
CI IDS
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
PRP (Properties); USES (Uses)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

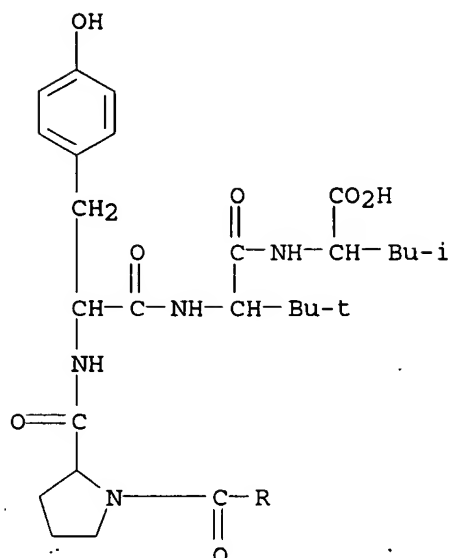
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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L7 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN
RN 579449-01-7 REGISTRY
CN L-Leucine, (2S)-2-[1-[[[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5(or 6)-yl]amino]thioxomethyl]-4-piperidinyl]glycyl-L-prolyl-(2S)-2-[1-(aminoiminomethyl)-4-piperidinyl]glycyl-L-arginyl-L-prolyl-L-tyrosyl-3-methyl-L-valyl- (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 8
NTE modified (modifications unspecified)

SEQ3 1 Gly-Pro-Gly-Arg-Pro-Tyr-Val-Leu
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HITS AT: 1-8

RELATED SEQUENCES AVAILABLE WITH SEQLINK

[illegible]



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

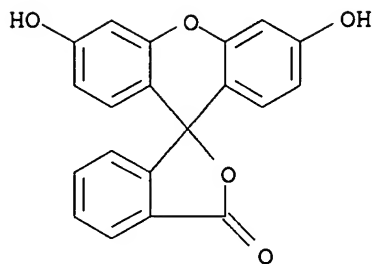
L7 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN
RN 579449-00-6 REGISTRY
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FS PROTEIN SEQUENCE
SQL 8
NTE modified (modifications unspecified)

SEQ3 1 Gly-Pro-Gly-Arg-Pro-Tyr-Val-Leu
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HITS AT: 1-8

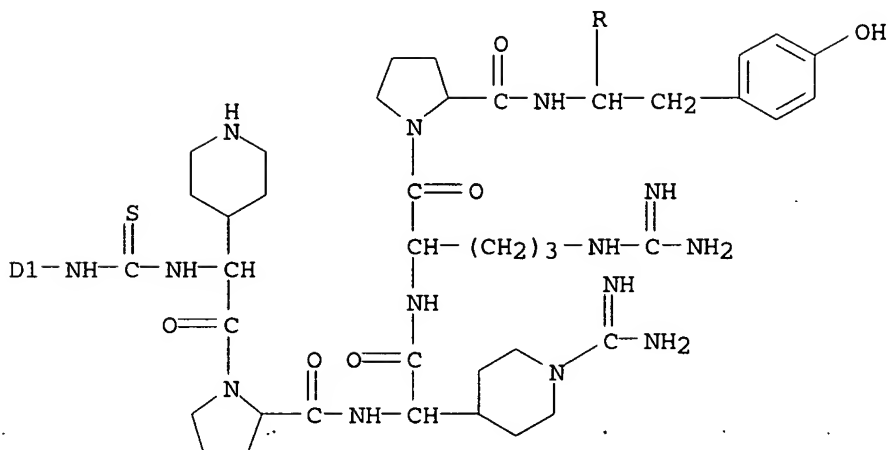
RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C73 H96 N16 O15 S
CI IDS
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA Caplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
PRP (Properties); USES (Uses)

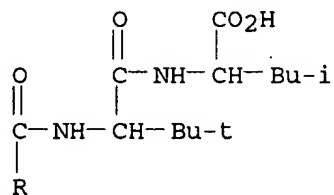
PAGE 1-A



PAGE 2-A



PAGE 3-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L7 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 579448-99-0 REGISTRY
 CN 6-13-Neurotensin (cattle), 6-[N2,N6-bis[[[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5(or 6)-yl]amino]thioxomethyl]-D-lysine]-8-[(2S)-2-[1-(aminoiminomethyl)-4-piperidinyl]glycine]- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE

SQL 8

NTE modified (modifications unspecified)

type	location	description
stereo	Lys-1	D

SEQ3 1 Lys-Pro-Gly-Arg-Pro-Tyr-Ile-Leu

=== === === === === === ===

HITS AT: 1-8

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C93 H107 N17 O20 S2

CI IDS

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA Caplus document type: Journal

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
PRP (Properties); USES (Uses)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L7 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN

RN 579448-98-9 REGISTRY

CN 6-13-Neurotensin (cattle), 6-[N6-[[[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5(or 6)-yl]amino]thioxomethyl]-D-lysine]-8-[(2S)-2-[1-(aminoiminomethyl)-4-piperidinyl]glycine]- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE

SQL 8

NTE modified (modifications unspecified)

type	location	description
stereo	Lys-1	D

SEQ3 1 Lys-Pro-Gly-Arg-Pro-Tyr-Ile-Leu

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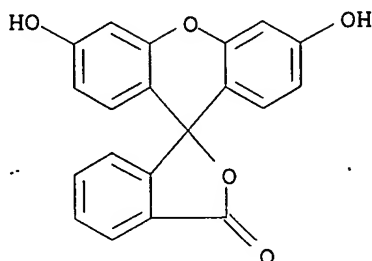
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RELATED SEQUENCES AVAILABLE WITH SEQLINK

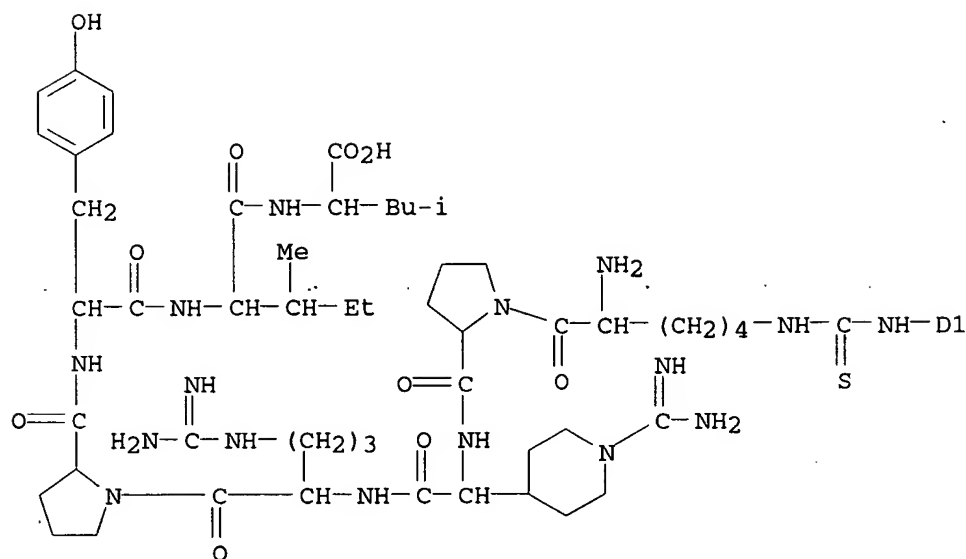
MF C72 H96 N16 O15 S

CI IDS
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER
 DT.CA CAPLUS document type: Journal
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
 PRP (Properties); USES (Uses)

PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L7 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN
 RN 579448-97-8 REGISTRY
 CN 6-13-Neurotensin (cattle), 6-[N2-[[[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5(or 6)-yl]amino]thioxomethyl]-D-lysine]-8-[(2S)-2-[1-(aminoiminomethyl)-4-piperidinyl]glycine]- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE

SQL 8

NTE modified (modifications unspecified)

type	location	description
stereo	Lys-1	D

SEQ3 1 Lys-Pro-Gly-Arg-Pro-Tyr-Ile-Leu

=== === === === ===

HITS AT: 1-8

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C72 H96 N16 O15 S

CI IDS

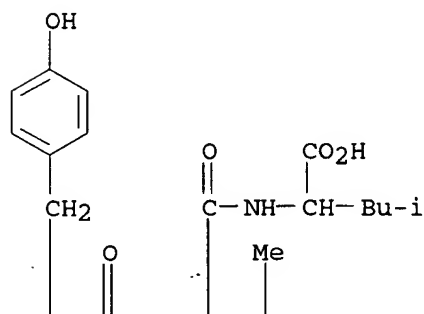
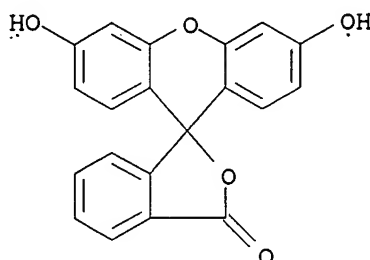
SR CA

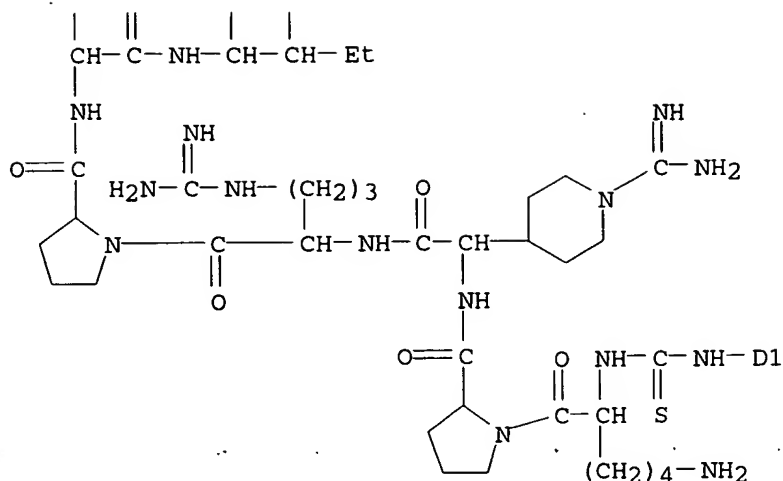
LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA Caplus document type: Journal

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation);
PRP (Properties); USES (Uses)

PAGE 1-A





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 13:51:51 ON 28 MAR 2005
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FILE COVERS 1907 - 28 Mar 2005 VOL 142 ISS 14
FILE LAST UPDATED: 27 Mar 2005 (20050327/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que 18
L2 714 SEA FILE=REGISTRY ABB=ON PLU=ON .P.RPY.L/SQSP
L5 2127679 SEA FILE=REGISTRY ABB=ON PLU=ON NC5/ES
L6 45 SEA FILE=REGISTRY ABB=ON PLU=ON L5 AND L2
L7 7 SEA FILE=REGISTRY ABB=ON PLU=ON L6 AND SQL=8
L8 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L7

=> d .ca 18 102

2 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
 ENTER ANSWER NUMBER OR RANGE (1):1-2

L8 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:575856 HCAPLUS

DOCUMENT NUMBER: 141:12065

TITLE: Stabilised 111In-labelled DTPA- and DOTA-conjugated
 neurotensin analogues for imaging and therapy of
 exocrine pancreatic cancer

AUTHOR(S): de Visser, M.; Janssen, P. J. J. M.; Srinivasan, A.;
 Reubi, J. C.; Waser, B.; Erion, J. L.; Schmidt, M. A.;
 Krenning, E. P.; de Jong, M.

CORPORATE SOURCE: Department of Nuclear Medicine, Erasmus MC, Rotterdam,
 3015 GD, Neth.

SOURCE: European Journal of Nuclear Medicine and Molecular
 Imaging (2003), 30(8), 1134-1139

CODEN: EJNMA6; ISSN: 1619-7070

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 28 Jul 2003

AB Neurotensin (NT) receptors are overexpressed in exocrine pancreatic cancer and Ewing's sarcoma. The potential utility of native NT in cancer diagnosis and therapy is, however, limited by its rapid degradation in vivo. Therefore, NT analogs were synthesized with modified lysine and arginine derivs. to enhance stability and coupled either to DTPA, to enable high specific activity labeling with indium-111 for imaging, or to DOTA, to enable high specific activity labeling with β -emitting radionuclides, such as lutetium-177 and yttrium-90. Based on serum stability (4 h incubation at 37°C in human serum) and receptor binding affinity, the five most promising analogs were selected and further evaluated in in vitro internalization studies in human colorectal adenocarcinoma HT29 cells, which overexpress NT receptors. All five NT analogs bound with high affinity to NT receptors on human exocrine pancreatic tumor sections. The analogs could be labeled with 111In to a high specific activity. The 111In-labeled compds. were found to be very stable in serum. Incubation of HT29 cells with the 111In-labeled analogs at 37°C showed rapid receptor-mediated uptake and internalization. The most promising analog, peptide 2530 [DTPA-(Pip)Gly-Pro-(PipAm)Gly-Arg-Pro-Tyr-tBuGly-Leu-OH] was further tested in vivo in a biodistribution study using HT29 tumor-bearing nude mice. The results of this study showed low percentages of injected dose per g tissue of this 111In-labeled 2530 analog in receptor-neg. organs like blood, spleen, pancreas, liver, muscle and femur. Good uptake was found in the receptor-pos. HT29 tumor and high uptake was present in the kidneys. Co-injection of excess unlabeled NT significantly reduced tumor uptake, showing that tumor uptake is a receptor-mediated process. With their enhanced stability, maintained high receptor affinity and rapid receptor-mediated internalization, the 111In-labeled DTPA- and DOTA-conjugated NT analogs are excellent candidates for imaging and therapy of exocrine pancreatic cancer, peptide 2530 being the most promising analog.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 8

IT 67-43-6DP, Dtpa, radiolabeled neurotensin analog conjugates

15750-15-9DP, Indium-111, neurotensin analogs labeled with, biological
 studies 39379-15-2DP, Neurotensin, radiolabeled analogs 60239-18-1DP,

Dota, radiolabeled neurotensin analog conjugates 328526-76-7P
 694452-76-1DP, In(111)-labeled 697236-75-2P 697236-79-6P
 697236-89-8P 697236-90-1P
 RL: DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(stabilized 111In-labeled DTPA- and DOTA-conjugated neurotensin analogs
 for imaging and therapy of exocrine pancreatic cancer)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:469885 HCAPLUS

DOCUMENT NUMBER: 139:185489

TITLE: Novel Bioactive and Stable Neurotensin Peptide Analogs
 Capable of Delivering Radiopharmaceuticals and
 Molecular Beacons to Tumors

AUTHOR(S): Achilefu, Samuel; Srinivasan, Ananthacari; Schmidt,
 Michelle A.; Jimenez, Hermo N.; Bugaj, Joseph E.;
 Erion, Jack L.

CORPORATE SOURCE: Mallinckrodt Institute of Radiology, Washington
 University School of Medicine, St. Louis, MO, 63110,
 USA

SOURCE: Journal of Medicinal Chemistry (2003), 46(15),
 3403-3411

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 20 Jun 2003

AB The prevalence of neurotensin receptor (NTR) in several human tumors makes
 it an attractive target for the delivery of cytotoxic drugs and imaging
 agents. Native neurotensin (NT) is a tridecapeptide that binds to NTR and
 induces tumor growth. Unfortunately, NT has a short plasma half-life,
 which hinders its use for in vivo biomedical applications. Numerous
 reports suggest that Arg(8)-Arg(9) and Tyr(11)-Ile(12) amide bonds are
 particularly susceptible to degradation by proteolytic enzymes. Predicated on
 this observation, we substituted Arg(8), Arg(9), and Ile(12) amino acids
 with the corresponding com. available mimics. These surrogate amino acids
 are amenable to standard Fmoc peptide synthesis strategy, and the resulting
 compds. are stable in biol. media for >4 h and bind to NTR with high
 affinity. Furthermore, conjugating DTPA to the new peptides and
 subsequent labeling with 111In-DTPA for nuclear imaging or fluorescein for
 optical imaging did not diminish the NTR binding affinities of the
 peptides. In vivo biodistribution of a representative 111In-DTPA-NT
 peptide analog in SCID mice bearing NTR-pos. human adenocarcinoma (HT29)
 xenograft shows that the compound was primarily retained in tumor tissue
 (2.2% ID/g) and the kidneys (4.8% ID/g) at 4 h postinjection. Coinjection
 of cold NT and the radiolabeled NT peptide analog inhibited the tumor but
 not the kidney uptake, demonstrating that retention of the radiolabeled
 compound in tumor tissue was mediated by NTR specific uptake while it
 accumulates in the kidneys by a nonspecific mechanism. These findings
 show that the new NT peptide analogs are robust and can deliver imaging
 agents to NTR-pos. tumors such as pancreatic cancer.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 34

IT	202843-05-8P	578719-67-2P	578719-69-4P	578719-72-9P	578719-74-1P
	578719-76-3P	578719-80-9P	578719-82-1P	578719-84-3P	578719-86-5P
	578719-88-7P	578719-90-1P	578719-92-3P	578719-94-5P	578719-96-7P

Mohamed 10/036,918

578719-98-9P 578720-00-0P 578720-02-2P 578720-04-4P 578720-06-6P
578720-08-8P 578720-10-2P 578720-12-4P **579448-97-8P**
579448-98-9P 579448-99-0P 579449-00-6P
579449-01-7P 579449-02-8P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)

(novel bioactive and stable neurotensin peptide analogs capable of
delivering radiopharmaceuticals and mol. beacons to tumors)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>